AMENDMENTS TO THE SPECIFICATION

Replace the paragraph beginning at page 2, line 23 with:

The regulatory effect of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide on the blood glucose level has been revealed experimentally in alloxan diabetes. It is believed that alloxan diabetes is associated with the injury of the β-cells of the pancreas and is accompanied by the pronounced hyperglycaemia due to insulin deficiency and glyconeogenesis activation.

Replace the paragraph beginning at page 2, line 27 with:

The tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] was experimentally proved to be non-toxic.

Replace the paragraph beginning at page 2, line 32 with:

The notion "pharmaceutical substance" under this application implies the use of any drug form containing the effective amount of the tetrapeptide of the general formula Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] which can find its preventive and/or therapeutic employment in medicine as a substance regulating blood glucose level in case of diabetes mellitus.

Replace the paragraph beginning at page 3, line 16 with:

The proposed invention also refers to the method of prevention and/or treatment of diabetes mellitus, which consists in administering to the patient of the pharmacological substance, containing as an active peptide agent an effective amount of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] in doses of 0.1 -30 μg/kg of the body weight at least once a day during the period necessary to obtain therapeutic effect.

Replace the paragraph beginning at page 3, line 32 with:

Table 1 demonstrates the effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on blood glucose level of the rats with alloxan diabetes (treatment).

Replace the paragraph beginning at page 3, line 34 with:

Table 2 demonstrates the effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on blood glucose level of the rats with alloxan diabetes (prevention and treatment).

Replace the paragraph beginning at page 4, line 1 with:

Table 3 demonstrates the effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] in different doses on blood glucose level of the rats with alloxan diabetes.

Replace the paragraph beginning at page 4, line 3 with:

Table 4 demonstrates the effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on insulin level in blood of the rats with alloxan diabetes.

Replace the paragraph beginning at page 4, line 5 with:

Table 5 demonstrates the results of the glucose tolerance test in the rats with alloxan diabetes (the 44^{th} day after the tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] course completion).

Replace the paragraph beginning at page 4, line 7 with:

Table 6 demonstrates insulin effect on blood glucose level of the rats with alloxan diabetes (the 28^{th} day after the tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] course completion).

Replace the paragraph beginning at page 4, line 10 with:

Table 8 demonstrates the effectiveness of the tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] parenteral administration to patients, suffering type 1 and type 2 diabetes mellitus, who were treated with insulin.

Replace the paragraph beginning at page 4, line 13 with:

The proposed invention is illustrated by the example of the tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] synthesis (~~Example1~~ Example 1), by the examples of the tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] biological activity (examples 2, 3, 4, 5, 6,

7), and by the example of the results of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] clinical application, which demonstrates its pharmacological properties and confirms the possibility to achieve prophylactic or/and treatment effect (example 8).

Replace the paragraph beginning at page 4, line 19

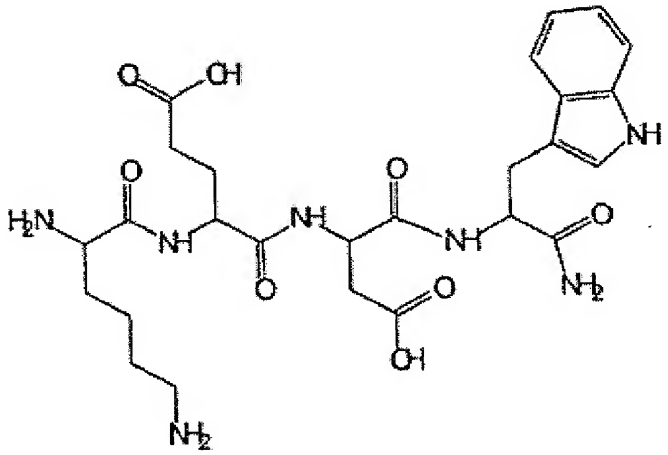
Example 1. Synthesis of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide

Replace the paragraph beginning at page 4, line 21 with:

1. Product name: lysyl-glutamyl-aspartyl-tryptophane amid [SEQ ID NO:1]

Replace the paragraph beginning on page 4, lines 22 -30

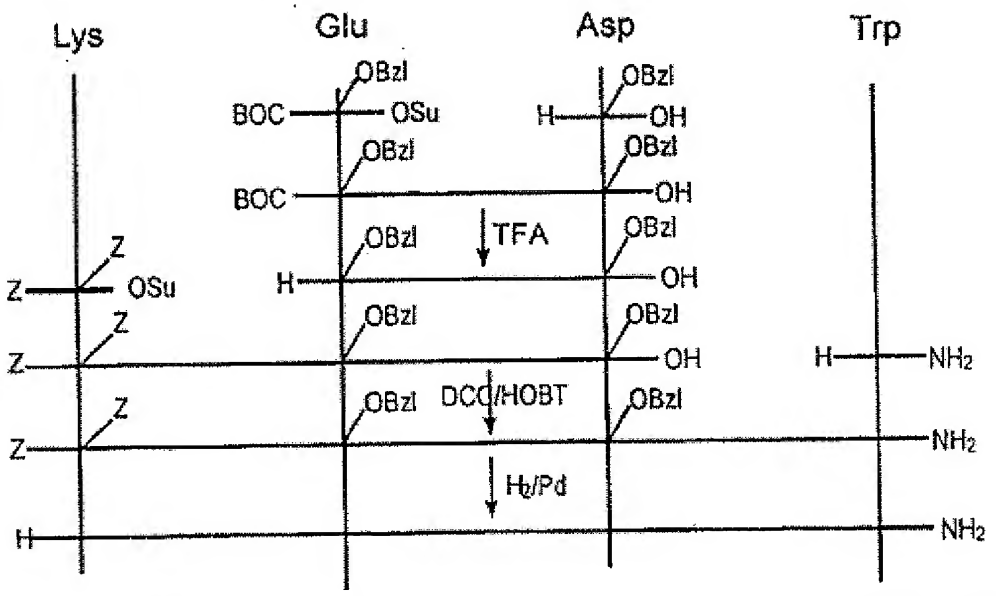
2. Structural formula:



H-Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]

Replace the graph beginning on page 5, lines 1-21 with:

7. Method of synthesis: the peptide is obtained by a classical method of synthesis in a solution by the following scheme:



[SEQ ID NO: 1]

Z – benzyloxycarbonyl group;
BOC – tert.butyloxycarbonyl group;
OSu – N-oxysuccinimide ester;
OBzl – benzyl ester;
DCC – N,N'-dicyclohexylcarbodiimide;
HOBT – N-oxybenzotriazol.

Replace the paragraph beginning at page 7, line 4 with:

4. ~~Z-Lys(Z)-Glu(OBzl)-Asp(OBzl)-Pro-OBzl~~ Z-Lys(Z)-Glu(OBzl)-Asp(OBzl)-Trp-NH_2 [SEQ ID NO: 2] (IV), 1024,15 N,N^{ε}-dibenzyloxycarbonyllysyl-(γ-benzyl)glutamyl-(β-benzyl)aspartyl-tryptophan amid.

Replace the paragraph beginning at page 7, line 19 with:

5. H-Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] (V), lysyl-glutamyl-aspartyl-triptophane amid, 575,62

Replace the paragraph beginning at page 7, line 20 with:

4.7 g of N,N$^{\varepsilon}$-dicarbobenzenoxylysyl-(γ-benzyl)glutamyl-(β-benzyl)aspartyl-triptophane amid (IV) [SEQ ID NO: 2] is hydrogenated in the methanol/water (5:1) system over Pd/C catalyst. Completeness of the deblocking reaction is monitored by TLC method in the benzene/acetone (2:1) and acetonitrile/water (1:3) systems. At the reaction completion the catalyst is filtered out, the filtrate is removed *in vacuo* and the residue is recrystallised in the water/methanol system. The product is dried *in vacuo* over KOH. The yield is 2.6 g (90%). $R_f = 0.64$ (acetonitrile/water, 1: 1).

Replace the paragraph beginning at page 8, line 12 with:

Example 2. Effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on the course of alloxan diabetes in rats (treatment variant)

Replace the paragraph beginning at page 8, line 14 with:

The study was conducted on 21 white mongrel male rats with average body weight 375±35 g. After estimation of glucose concentration in the blood all the animals were divided at random into 2 groups. Then all the animals were exposed to single intravenous administration 1 ml of alloxan solution ("Spofa") in dose 35 mg/kg. In 15 days control animals were administered once a day intraperitoneally with 0,3 ml 0,9% NaCl solution, rats of the main group were administered with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] in dose 3 μg (in 0,3 ml of 0,9% NaCl solution) per rat during 11 days.

Replace the paragraph beginning at page 8, line 20 with:

Table 1 shows the results of the study which reveal that Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide administration contributed to the reliable decrease of the blood glucose level in the animals throughout the whole study by 38,4% (30-47,7%). Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide-related glucose level decrease correlated with the lethality decrease in animals of the main group. So in the animals of the control group by the end of the investigation (84 days after alloxan administration) lethality was 70%, while in the rats which were administered with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide - 36,4%. Thus the Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide administration enabled two-fold lethality decrease in alloxan diabetes animals.

Replace the paragraph beginning at page 8, line 29 with:

Example 3. Effect of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on the course of alloxan diabetes in rats (prophylaxis and treatment variant)

Replace the paragraph beginning at page 8, line 32 with:

The experiment was carried out on 15 white mongrel male rats with the average body weight 375±35 g. The animals were divided randomly into 2 groups. Control animals were administered once a day intravenously with 0,3 ml of 0,9% NaCl solution, while the main group animals were administered with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in dose of 3 μg (in 0,3 ml of 0,9% NaCl solution) per rat during 7 days. After that all the animals were subject to single intravenous administration of 1 ml of alloxan solution ("Spofa") in dose 35 mg/kg. Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide had been administered during 3 days following alloxan administration. After that control rats were subject to the second Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide course from 18 day till day 28 (total 11 days) in the same dose.

Replace the paragraph beginning at page 9, line 5 with:

The results of the study are shown in table 2. First of all, it should be mentioned that Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide administration to healthy animals did not lead to the decrease of blood glucose level. Control animals during the whole experimental period after alloxan administration revealed diabetes mellitus development accompanied by the increased glucose concentration in the blood 1,9-4,9 times as compared to initial level. The rats subjected to one course of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide revealed a decrease of blood glucose level by 22-30% as compared to the controls. After the second course of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide these animals revealed a complete normalisation of the blood glucose level in all experimental periods (the 28^{th}, 33^{rd}, 40^{th} day), while in the animals of the control group the blood glucose level was correspondently 2; 4.2;3.8 fold increased.

Replace the paragraph beginning at page 9, line 15 with:

It should be noted, that only 2 rats out of 8 treated with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide reported severe form of diabetes mellitus, while in the control group there were 5 rats out of 7, thus, in the control group this index was ~~2,9fold~~ 2.9 fold higher.

Replace the paragraph beginning at page 9, line 18 with:

On completion of the study (the 40^{th} day after alloxan administration), there survived 57.1% of the control animals and 75% of the animals treated with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide.

Replace the paragraph beginning at page 9, line 20 with:

The results of the study show that Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide contributes to the normalisation of the glucose level in alloxan diabetes rats, which is accompanied by the decrease of lethality.

Replace the paragraph beginning at page 9, line 24 with:

Example 4. Effect of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in different doses on the course of alloxan diabetes in rats

Replace the paragraph beginning at page 9, line 30 with:

Then the animals were divided at random into 3 groups. Control animals were intraperitoneally administered with 0.3 ml of 0.9% NaCl solution once a day. Rats of the second and third group were administered with tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] in dose of 1 μg (in 0.1 ml of 0.9% NaCl solution) and 10μg (in 1,0 ml of 0.9% NaCl solution) per rat during 7 days.

Replace the paragraph beginning at page 9, line 34 with:

Table 3 demonstrates the results of this experiment. The administration of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] to rats in dose of 1μg contributed to the pronounced increase in the blood glucose level on the 1^{st} and the 4^{th} days after completion of the tetrapeptide course by 17,3 and 12,3% correspondingly as compared to the controls. Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] administration to rats in dose of 10 μg

led to even more pronounced decrease of glucose level by 30; 23.8; 26; 12.7% on day 1, 4, 7, 17 correspondingly. These data show that the increase of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] dose pronouncedly effects on blood glucose level of animals.

Replace the paragraph beginning at page 10, line 7 with:

Example 5. Effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on blood glucose level of alloxan diabetes rats

Replace the paragraph beginning at page 10, line 9 with:

The experiment was held on 18 white mongrel rats weighing an average 375±35 g. After the estimation of the blood glucose level all the animals were divided at random into 2 groups. Then all the animals were subjected to single intravenous injection with 1 ml of alloxan solution ("Spofa") in dose of 35 mg/kg. 15 days later control animals were daily ~~intraperitonealy~~ intraperitoneally administered with 0.3 ml of 0.9% NaCl solution, rats of the main group – with tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] in dose of 3 μg (in 0.3 ml of 0.9% NaCl) per rat during 11 days.

Replace the paragraph beginning at page 10, line 15 with:

The results of the experiment are represented in table 4, which demonstrates that on day 15 after alloxan administration the animals reported diabetes mellitus. In the rats administered with tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] insulin content in the blood during 8 days after the substance had been administered was 3,9 fold higher than in rats of the control group. All the following estimations conducted during the experiment revealed some amount of insulin in the blood of the rats (13-18%), though there was no insulin at all in the blood of the control animals. On completion of the experiment (on the 70^{th} day after alloxan administration) 62,5% of the control animals were alive, in the animals administered with tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] 70% were alive.

Replace the paragraph beginning at page 10, line 23 with:

The analysis of the results of this experiment showed that administration of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] to animals with alloxan diabetes

contributes to the maintenance of the insulin blood level, which can result from the partial restoration of the insulin producing cell structure and function.

Replace the paragraph beginning at page 10, line 29 with:

Example 6. Effect of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] on indices of sugar curve in alloxan diabetes rats (treatment variant)

Replace the paragraph beginning at page 10, line 31 with:

The study was conducted on 13 male rats, enrolled in the previous tests (treatment variants – 44 days after completion of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] administration). 7 healthy rats with the same body weight constituted a separate group. All the animals were administered intravenously with 1 ml of 2% glucose solution, after that glucose concentration in their blood was estimated.

Replace the paragraph beginning at page 10, line 36 with:

Table 5 demonstrates the results of the trial, which reveal that in healthy rats after glucose administration its concentration was 5 min later – 203.9%, 30 min – 156.3%, 60 min – 124.6%, 120 min – 114.5% compared to the initial level (100%). In control animals the same index was correspondingly 129.8; 127.5; 123.5; 121.1%. These data point at the strong suppression of the pancreas function after alloxan lesion. The same index in rats, which were administered with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide was 142.9; 97.3; 95.6; 77.9%. The results of this trial reveal that Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide can stimulate pancreas function in rats, suffering alloxan diabetes.

Replace the paragraph beginning at page 11, line 10 with:

Example 7. Insulin effect on blood glucose level in alloxan diabetes rats after Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide administration.

Replace the paragraph beginning at page 11, line 13 with:

The study was conducted on 13 male rats, enrolled in the previous trial (treatment variant – 28 days after completion of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide

administration). 8 healthy rats of the similar body weight constituted a separate group. All the animals were administered intravenously with insulin (0,3 units) and glucose concentration in their blood was estimated hereafter.

Replace the paragraph beginning at page 11, line 18 with:

The results of the study are shown in table 6. Healthy animals revealed a strong physiological decrease in glucose level, while in control animals (suffering alloxan diabetes) this index was 2,8 times lower. Alloxan diabetes animals treated with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide, revealed a reliable nearly two-fold decrease of the glucose level after insulin administration as compared to the control group. These data suggests Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide ability to a great extent maintain tissue sensibility to insulin.

Replace the paragraph beginning at page 11, line 24 with:

The properties of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide revealed during the study allow to recommend it for prophylactic and therapeutic application as a substance regulating blood glucose level in case of diabetes mellitus treatment.

Replace the paragraph beginning at page 11, line 30 with:

Example 8. Efficacy of applying Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in the patients with diabetes mellitus.

Replace the paragraph beginning at page 11, line 32 with:

The investigation was carried out in 36 patients aged from 16 to 83 years (7 men, 29 women). In 23 patients there was diagnosed type 1 diabetes, in 13 patients – type 2 diabetes. The disease duration varied from 1 year to 30 years. 32 patients received insulin. The majority of the patients suffering diabetes mellitus entered the hospital decompensated. Blood glucose level in these patients on an empty stomach oscillated from 9.5 to 27 μm/l; the glycosylated haemoglobin – from 7.8 to 12.7%. All the patients were prescribed a rigid diet. All the patients were stratified randomly into 2 groups, with respect to age, sex, duration and stage of the disease (Table 7). Alongside with standard method of treatment 16 patients were prescribed Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in dose of 10μg (in 1 ml of

0.9% NaCl solution) intramuscularly once a day for 10 days. 4 patients suffering type 2 diabetes mellitus were prescribed together with standard treatment course Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in dose of 100 μg (1 tablet) twice a day before meals during 10 days. Patients of the control group were administered with 1 ml of 0,9% of NaCl solution as a placebo following the same scheme.

Replace the paragraph beginning at page 12, line 8 with:

The results of the study of the Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide efficacy are shown in Table 8. In 8 patients (out of 16 treated insulin) Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide course resulted in reduction of the insulin daily dose by 8 units on average, this allowed to achieve the compensation.

Replace the paragraph beginning at page 12, line 18 with:

In patients of the main group suffering ~~type 2diabetes~~ type 2 diabetes mellitus (1 patient) and type 1 diabetes mellitus (3 patients), who received Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in tablets daily, the dose of insulin was reduced by 25 units and in patients, who were treated with oral anti-diabetic medicine, there was achieved a full compensation and the dose of preparations was reduced practically two-fold.

Replace the paragraph beginning at page 12, line 23 with:

Thus, the application of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide in patients suffering diabetes mellitus contributed to the increase of tissues sensitivity towards insulin and to some extent to pancreas function restoration. It should be noticed that there was registered rather high effectiveness of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide, which was evidenced by the decrease of insulin dose in 50% of patients of the main group, while none of the patients in control group revealed this result.

Replace the paragraph beginning at page 13, line 4 with:

Therapy: diet, vitamins of B group, berlition, parenteral form of the pharmaceutical composition, containing Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide, 10 μg intramuscularly during 10 days.

Replace the paragraph beginning at page 13, line 17 with:

Therapy: diet, vitamins of B group, parenteral form of the pharmaceutical composition, containing Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide, 10 μg intramuscularly during 10 days.

Replace the paragraph beginning at page 13, line 26 with:

On admission for treatment: blood glucose level on an empty stomach – 11 μmol/l. Clinical blood and urine analysis – normal. Takes 2 tab. of diabeton daily. As the patient had revealed resistance towards pilled antidiabetic preparations she was recommended to take insulin. But the patient declined to be treated with insulin, that was why she was prescribed oral form of pharmaceutical composition, containing Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide, 100 μg (1 tab) twice a day before meals during 10 days together with the intake of 2 diabeton tablets. On the second day glucose level on an empty stomach was 6 μmol/l. Then the dose of diabeton was reduced two-fold. After the completion of the treatment course with Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO:1] tetrapeptide the blood glucose level remained within the norm. Present state of the patient is satisfactory.

Replace Table 1 page 14, with:

Table 1

Animal Group	Glucose Concentration in the blood (mg %)								
	Initial level	15 days after alloxan administration	8 days since the onset of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide administration	Upon completion of peptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] administration (days)					
				1	9	18	28	44	58
Control (NaCl)	84.0±5.7	345.0±15.4	360.0±12.3	342.5±17.3	351.4±11.2	368.3±8.1	375.7±12.8	347.2±12.8	332.1±13.7
n	10	10	9	8	7	6	5	5	3
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]	81.1±3.8	333.6±12.4	254.5±16.2	222.5±10.3*	183.9±10.5*	236.7 ± 10.3*	221.5±11.2*	210.8±9.3*	198.9±11.5*
n	11	11	11	10	9	9	8	8	7

* - P<0.001 as compared to the control.

Replace Table 2 at page 15 with:

Table 2

Animal Group	Glucose Concentration in the blood (mg %)							
	Initial level	7 days from the onset of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide administration (1 course)	After alloxan administration (days)					
			5	14	18	28	33	40
					2nd course of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide administration (from 18th till 28th day)			
Control (NaCl)	82.7±0.9	96.4±1.0	351.7±19.4*	333.7±55.8*	345.6±57.8*	156.4±26.4*	383.0±89.3*	405.0±89.8*
n	7	7	7	6	5	5	4	4
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]	76.8±1.1	94.0±0.8	247.3 ± 17.2*#	261.5±39.5*#	159.0±32.6*#	77.3±1.3#	90.7±5.2#	107.7±6.4#
n	8	8	8	8	6	6	6	6

* - P<0.001 as compared to the control;

- P<0.02 as compared to the control.

Replace Table 3 at page 16 with:

Table 3

Animal Group	Glucose Concentration in the blood (mg %)							
	Initial level	After alloxan administration (days)		After Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide administration (days)				
		7	14	1	4	7	14	21
Control (NaCl)	78.6 ± 4.2	276.4 ± 0.9	272.1 ± 9.8	275.7 ± 9.7	278.6 ± 9.8	277.9 ± 11.1	275.0 ± 10.5	285.0 ± 12.9
n	7	7	7	7	7	7	6	6
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] (1 mkg)	80.6 ± 2.8	245.6 ± 12.3	261.7 ± 12.3	228.3 ± 10.7*	244.4 ± 12.2*	269.4 ± 8.6	268.8 ± 12.4	272.5 ± 9.9
n	9	9	9	9	8	8	8	8
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] (10 mkg)	83.9 ± 3.4	247.2 ± 14.0	252.2 ± 7.9	193.3 ± 6.7*	212.2 ± 7.3*	205.6 ± 8.4*	240.0 ± 7.9*	248.3 ± 13.5
n	7	7	7	7	7	7	6	6

* - $P<0.05$ as compared to the control.

Replace Table 4 at page 17 with:

Table 4

Animal Group	Insulin content in blood (mkIU/ml)							
	Initial level	15 days after alloxan administration	8 days since the onset of Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] tetrapeptide administration	After the completion of tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1] administration (days)				
				1	9	18	28	44
Control (NaCl)	24.3 ± 2.1	2.0 ± 0.7	0.8 ± 0.25	0	0	0	0	0
n	8	8	8	7	6	5	5	5
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]	23.8 ± 2.8	1.5 ± 0.4	3.1 ± 1.1*	3.6 ± 0.7#	3.2 ± 0.5#	4.3 ± 0.5#	4.1 ± 0.6#	3.9 ± 1.1#
n	10	10	10	8	7	7	7	7

* - P<0.05 as compared to the control

- P<0.001 as compared to the control.

Replace Table 5 at page 18 with:

Table 5

Animal Group	Initial Level	Time after glucose administration (min)			
		5	30	60	120
Healthy	84.5 ± 4.2	172.3 ± 8.1	132.1 ± 9.1	105.3 ± 6.2	96.8 ± 5.3
n	7	7	7	7	7
Control (NaCl)	347.2 ± 12.8*	450.5 ± 15.2*	442.7 ± 14.3*	428.9 ± 14.1	420.5 ± 16.5
n	5	5	5	5	5
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]	210.8 ± 9.3#	301.2 ± 10.5#	205.1 ± 11.8#	201.5 ± 13.2#	164.2 ± 12.8#
n	8	8	8	8	8

* - P<0.001 as compared to healthy animals;
# - P<0.05 as compared to the control.

Replace Table 6 at page 19 with:

Table 6

Animal Group	Glucose concentration in blood (mg%)		Decrease in glucose content with respect to intial level (%)
	Initial Level	30 minutes after insulin administration	
Healthy	83.5 ± 3.2	29.4 ± 2.2	64.8
n	8	8	
Control (NaCl)	35.7 ± 11.2*	287.8 ± 12.5*	23.4
n	5	5	
Tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1]	221.5 ± 11.2#	123.6 ± 8.3#	44.2
n	8	8	

* - P<0.001 as compared to healthy animals;
# - P<0.05 as compared to the control.

Replace Table 7 at page 20 with:

Table 7

Index	Group of patients	
	Control (placebo)	Main (tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1])
Number of patients	16	20
Men	3	4
Women	13	16
Number of patients with type 1 diabetes mellitus	11	12
Number of patients with type 2 diabetes mellitus	5	8

Replace Table 8 at page 20 with:

Table 8

Index	Group of patients	
	Control (placebo)	Main (tetrapeptide Lys-Glu-Asp-Trp-NH_2 [SEQ ID NO: 1])
Number of patients	16	16
Decreased insulin dose necessary to achieve compensation	0	8
The same insulin dose necessary to achieve compensation	2	6
Increase insulin dose necessary to achieve compensation	14	2